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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/600,493	07/18/2000	Jack Wands	MGH-0026	3498

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EXAMINER
SHUKLA, RAM R

ART UNIT	PAPER NUMBER
1632	17

DATE MAILED: 09/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/600,493	WANDS ET AL.	
	Examiner	Art Unit	
	Ram R. Shukla	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6-30-03* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,4,6,17-28 and 34-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,4,6,17-28 and 34-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 July 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *15* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The after-final amendment and response filed 6-30-03 have been received and entered.

2. Claims 11-16, 32, 33, and 39-46 have been cancelled.

3. Claims 3, 4, 6, 17-28, and 34-38 are under consideration.

4. The information provided in the Ref# 51 listed in the supplementary IDS filed 4-15-03 has been considered, however, the reference can not be printed since it does not have a publication date.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 3, 4, 6, 8, 17-18, 34, 36 and 38 are rejected under 35 U.S.C. 102(b) as being anticipated by Maertens et al (Maertens et al. WO 96/13590, 9 May 1996).

Maertens et al teaches a recombinant expression vector comprising a polynucleotide comprising sequences that express NS4, NS5 and also comprise 5' UTR of hepatitis C virus (see the entire document, particularly, see claims 7, 8, 28, 29 and pages 15, 23, 25, 32-33, 41, 43-44). The vector comprises control elements for expression in eukaryotic cells as discussed in the specification. Accordingly, the claimed invention is anticipated by Maertens et al.

7. Claims 3, 4, 6, 8, 17-18, 34, 36 and 38 are rejected under 35 U.S.C. 102(e) as being anticipated by Maertens et al (US 2002/0183508 A1, December 5, 2002).

Maertens et al teaches a recombinant expression vector comprising a polynucleotide comprising sequences that express NS4, NS5 and also comprise 5' UTR of hepatitis C virus (see the entire document, particularly, see claims 7, 8, 26-29 and paragraphs 0051, 0130, 0217, 0241, 0286). The vector comprises control elements for expression in eukaryotic cells as discussed in the specification. Accordingly, the claimed invention is anticipated by Maertens et al.

8. Claims 3, 4, 6, 8, 17-18, 34, 36 and 38 are rejected under 35 U.S.C. 102(b) as being anticipated by Donnelly et al (WO 97/47358, 18 December 5, 1997).

Donnelly et al teach synthetic hepatitis C genes, pharmaceutical compositions and formulation for vaccination and gene therapy and method of immunization (see the entire document). Particularly the art teaches DNA constructs that encode hepatitis C NS5 gene or any other HCV gene that generates specific immune responses in animal s(see 17-31 on page 3, figures 12 and 13, page 13-20, lines 12-17 page 20, claims 1, 8-23, 25-26). Accordingly, the claimed invention is anticipated by Donnelly et al.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions

covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 17, 18, 20-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maertens et al (Maertens et al. WO 96/13590, 9 May 1996) or Maertens et al (Maertens et al. US 2002/0183508 A1, December 5, 2002) or Selby et al (J. Gen.Virol. 74:1103-1113, 1993) or Donnelly et al (WO 97/47358, 18 December, 1997) in view of Tokushige et al Hepatology 24:14-20, 1996) and Ferrari et al (Hepatology 19:286-295).

Maertens et al (WO document) teaches a recombinant expression vector comprising a polynucleotide comprising sequences that express NS4, NS5 and also comprise 5' UTR of hepatitis C virus (see the entire document, particularly, see claims 7, 8, 28, 29 and pages 15, 23, 25, 32-33, 41, 43-44). The vector comprises control elements for expression in eukaryotic cells as discussed in the specification.

Maertens et al (US Pre-grant publication) teaches a recombinant expression vector comprising a polynucleotide comprising sequences that express NS4, NS5 and also comprise 5' UTR of hepatitis C virus (see the entire document, particularly, see claims 7, 8, 26-29 and paragraphs 0051, 0130, 0217, 0241, 0286). The vector comprises control elements for expression in eukaryotic cells as discussed in the specification. These arts by Maertens et al do not teach a method of producing an immune response in an animal by administering a nucleic acid comprising a nucleic acid encoding a hepatitis C virus nonstructural protein or combination.

Selby et al teaches several constructs for expression of viral proteins. For example, the plasmid pHCV comprises the entire viral genome (see the methods section on page 1103, right column continued into the left column on page 1104 and figure 1). The plasmids pHCV5-1 and pHCV comprise the entire 5'UTR and 3'UTR and the coding sequence for the non-structural proteins. Since the protein of

the virus is produced as a polyprotein, a fusion of NS4-NS5 would be produced as a result of partial proteolytic digestion.

Donnelly et al teach synthetic hepatitis C genes, pharmaceutical compositions and formulation for vaccination and gene therapy and method of immunization (see the entire document). Particularly the art teaches DNA constructs that encode hepatitis C NS5 gene or any other HCV gene that generates specific immune responses in animal s(see 17-31 on page 3, figures 12 and 13, page 13-20, lines 12-17 page 20, claims 1, 8-23, 25-26).

Tokushige et al teaches a method of producing immune response to hepatitis c virus core protein using a DNA based vaccine construct. The construct comprises a CMV promoter, an RSV enhancer, 5′ UTR of hepatitis c virus and the coding sequence for core protein. The art also teaches method of injecting the construct in a muscle and using bupivacaine (see the materials and methods section).

Ferrari et al teach T cell response to structural and non-structural hepatitis c virus antigens in persistent and self-limited hepatitis c virus infections. The art teaches that the core protein followed by the NS4 were the most potent T-cell immunogen for both chronic as well as asymptomatic anti-HCV-positive patients . The art also teaches that another paper taught that NS4 was the most immunogenic. The art also discusses role of other non-structural protein NS5.

Diepolder et al teach T cell response to the other non-structural hepatitis c protein N3 and note that TH0/TH1-like CD4T-lymphocyte response to NS3 and other nonstructural HCV proteins contributes to successful viral clearance, whereas the PBMC response to core protein may be more common in patients that develop chronic hepatitis C. They go on to suggest that NS3-specific CD4 T-cell response might be a candidate as a target for immunointervention in the treatment of acute, protracted and chronic hepatitis and for vaccine development.

At the time of the invention, it would have been obvious to an artisan of ordinary skill to modify the polynucleotides of Maertens et al, Selby et al or Donnely et al by cloning the non-structural protein encoding sequences in the vector of Tokushige et al or Donnelly et al to produce vectors that express HCV non-structural proteins alone or chimeric proteins and administer them to an animal and

produce immune response with a reasonable expectation of success. An artisan of skill would have been motivated to produce vectors that encode non-structural proteins or fusion of the non-structural proteins to find the best immunogen and use such for vaccination non-structural proteins were known in the art to be strongly immunogenic and the art of record suggested their potential use in developing vaccine and treatment and also because fusion proteins, such as core followed by NS-4 were most potent immunogens.

Applicant's arguments with respect to claims 3, 4, 6, 17-28 and 34-38 have been considered but are moot in view of the new ground(s) of rejection.

11. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for TC 1600 is (703) 703-872-9306. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the William Phillips whose telephone number is (703) 305-3413.

RAM R. SHUKLA, PH.D.
PRIMARY EXAMINER

Ram R. Shukla, Ph.D.
Primary Examiner
Art Unit 1632